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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/048,013	04/29/2002	Michael Luconi	LUCONI1	1351
1444 7590 09/26/2006 BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			EXAMINER WOOD, AMANDA P	
			ART UNIT 1655	PAPER NUMBER
DATE MAILED: 09/26/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/048,013	LUCONI ET AL.	
	Examiner	Art Unit	
	Amanda P. Wood	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-9,12,19,20 and 26-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-9,12,19,20 and 26-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment filed 18 July 2006 is acknowledged and has been entered.

Claims 1, 4-9, 12, 19, 20, and 26-28 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1, 4, 6, 7, 10, and 12 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nass-Arden et al (Mol. Reprod. Dev. 1990) for the reasons set forth in the previous office action which are restated below.

Nass-Arden et al teach a method wherein mammalian sperm (i.e., seminal liquid comprising spermatozoa) is treated with quercetin (i.e., an inhibitor of phosphatidylinositol 3-kinase) so as to increase the motility of the sperm. Nass-Arden et al further teach a method wherein the sperm are separated by sperm separation methods used in ART (i.e., assisted reproduction techniques), such as the wash and spin method, the sedimentation method, or the pellet and swim-up method.

Furthermore, Nass-Arden et al teach that in the first two hours of treatment with quercetin, motility is inhibited in sperm, but afterward, motility intensity and duration is enhanced. In addition, Nass-Arden et al teach that untreated sperm show no motility after 3.5 hours, whereas the sperm treated with the phosphatidylinositol 3-kinase

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inhibitor quercetin show high motility at this point, and continue to show high motility for an additional 2-3 hours. Furthermore, Nass-Arden et al teach that quercetin might be a good candidate to increase the fertilizing potential of spermatozoa (see, for example, Abstract, pg. 369, col. 2, pg. 370, col. 1, col. 2, and pg. 373, col. 1).

Therefore, the reference is deemed to anticipate the instant claims above.

Response to Arguments

Applicant's arguments filed 18 July 2006 have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the present invention teaches that motility is stimulated during the first two hours of incubation/treatment of seminal fluid with PI3K inhibitor) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Applicant argues that Nass-Arden teaches away from the present invention. However, the Examiner would like to point out that Nass-Arden teaches that "quercetin inhibits collective motility in the first two hours of incubation; during the next 3-4 hours motility is stimulated" (see, for example, Abstract). This teaching from Nass-Arden specifically reads on claim 1 of the instant application, wherein seminal liquid is treated for up to two hours with PI3K inhibitor sufficient to increase sperm motility. The instant application does recite claims to stimulation of motility during the first two hours of

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incubation/treatment with PI3K inhibitor. Therefore, the reference is still deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

Claims 1, 4-10, 12, and 19-29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nass-Arden et al in view of Vlahos et al (J. of Biol. Chem. 1994) and Bonjouklian et al (US 5,378,725) for the reasons set forth in the previous office action which are restated below.

Nass-Arden et al is relied upon for the reasons set forth above.

Vlahos et al beneficially teach that quercetin is a known inhibitor of phosphatidylinositol 3-kinase that is directed at the ATP-binding site of the kinase. Vlahos et al also beneficially teach that quercetin has also been shown to inhibit other phosphatidylinositols and protein kinases, which can be an unwanted side effect of using this particular inhibitor. For this reason, Vlahos et al teach that it would be beneficial to find other inhibitors of phosphatidylinositol 3-kinase that do not affect phosphatidylinositol 4-kinase or other selected protein kinases. Vlahos et al beneficially teach that 2-(4-morpholinyl)-8-phenyl-4H-1-benzopyran-4-one, or (LY294002), completely and specifically abolished phosphatidylinositol 3-kinase activity but did not inhibit any other tested protein or lipid kinases. Vlahos et al beneficially teach that LY294002 was efficacious in inhibiting phosphatidylinositol 3-kinase activity in

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whole cell assays (e.g., human neutrophils and sperm) as well as in purified phosphatidylinositol 3-kinase (see, for example, Abstract, pg. 5247, col. 2).

Bonjouklian et al beneficially teach that wortmannin and its analogs can be used in humans to inhibit phosphatidylinositol 3-kinase in lysed or whole cells.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method disclosed by Nass-Arden et al based upon the beneficial teachings provided by Vlahos et al, with respect to the art-recognized method of substituting one inhibitor for a more specific inhibitor, and by Bonjouklian et al, with respect to the fact that inhibitors of phosphatidylinositol 3-kinase for use in humans are well known in the art, as discussed above. Furthermore, Nass-Arden et al beneficially teach that quercetin treated sperm have greater motility for longer duration than untreated sperm, and that treatment with such a compound may increase the fertilizing potential of spermatozoa, and therefore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Nass-Arden et al to treat sperm so as to increase their motility. Bonjouklian et al teach that wortmannin and its analogs can be used in humans to inhibit phosphatidylinositol 3-kinase from both lysed and whole cells. Furthermore, Vlahos et al particularly teach that quercetin is a known inhibitor of phosphatidylinositol 3-kinase, and that it also inhibits other enzymes, which is an undesirable side effect. Vlahos et al further point out that it would be beneficial to find inhibitors of phosphatidylinositol 3-kinase that do not affect any other enzymes, and therefore, Vlahos et al teach that LY294002 is a specific inhibitor of phosphatidylinositol 3-kinase that is effective in whole-cell assays using

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human neutrophils. Based upon the beneficial teachings of Nass-Arden et al, Bonjouklian et al, and Vlahos et al, it would have been obvious to one of ordinary skill in the art to treat human seminal fluid comprising spermatozoa with a phosphatidylinositol 3-kinase inhibitor such as LY294002, wortmannin, or quercetin, or derivatives thereof and to use a method well-known in ART to separate the spermatozoa. In addition, based upon the known properties of these phosphatidylinositol 3-kinase inhibitors (i.e., the delayed onset of increased sperm motility), it would have been obvious to one of ordinary skill in the art to provide a medium for storage and/or transportation of mammalian spermatozoa comprising such an inhibitor, so as to provide a means for maximizing the sperm's motility upon arrival at the treatment clinic and/or upon the laboratory's need for the sperm in the ART procedure (i.e., IVF, GIFT, and IUI). Furthermore, it would have been both obvious and beneficial to one of ordinary skill in the art at the time the claimed invention was made to treat sperm being used in ART therapy using such inhibitors so as to increase the motility and fertilization potential of the sperm. The result-effective adjustment of particular conventional working conditions (e.g., using a particular amount of a particular phosphatidylinositol 3-kinase inhibitor, treating the sperm for a particular amount of time, and/or using a particular method of separation or ART therapy) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Response to Arguments

Applicant's arguments filed 18 July 2006 have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the present invention teaches that motility is stimulated during the first two hours of incubation/treatment of seminal fluid with PI3K inhibitor) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Applicant argues that Nass-Arden teaches away from the present invention. However, the Examiner would like to point out that Nass-Arden teaches that "quercetin inhibits collective motility in the first two hours of incubation; during the next 3-4 hours motility is stimulated" (see, for example, Abstract). This teaching from Nass-Arden specifically reads on claim 1 of the instant application, wherein seminal liquid is treated for up to two hours with PI3K inhibitor sufficient to increase sperm motility. The instant application does recite claims to stimulation of motility during the first two hours of incubation/treatment with PI3K inhibitor. Furthermore, Applicant argues that Vlahos and Bonjouklian do not cure the alleged deficiencies of Nass-Arden. However, based upon the above arguments that Nass-Arden clearly anticipates the claimed invention, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made to incorporate the teachings of Nass-Arden with that of both Vlahos and

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Bonjouklian to provide different inhibitors for use in treating seminal fluids for use in ART therapy for the expected benefit of maximizing sperm motility.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on M-F 8:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

APW
Examiner
Art Unit 1655

APW



CHRISTOPHER R. TATE
PRIMARY EXAMINER